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Title:

Impact of “eHealth” in Allergic Diseases and Allergic Patients

Running title:

“eHealth” and Allergy

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Abstract:

The emergence of new technology grants allergists and patients the opportunity to compile data and receive feedback regarding key symptoms, risk behaviour and/or management. The term “eHealth” refers to a diverse group of tools that use computerized technologies to improve efficacy and efficiency of the health care industry.

eHealth comprises a variety of technologies, such as the use of mobile devices (mHealth) in medical care, including electronic diaries, wearable sensors or adherence monitoring; health informatics (e.g. electronic health records, computerized physician order entry, clinical decision support); telemedicine, which is the use of information and communication technologies for the management of diseases and medical education; social media platforms, and the analysis of information acquired through these platforms using “big data” technologies.

In this review, we summarize the evidence surrounding use of eHealth technology and relevance to allergic conditions.

Keywords: big data; ehealth; mhealth; social media; telemedicine.

Resumen:

La aparición de nuevas tecnologías conlleva para los alergólogos y los pacientes la posibilidad de recopilar datos y recibir información directa sobre los síntomas clave de las enfermedades, los comportamientos de riesgo y/o su manejo. El término “eHealth”, o salud electrónica, se refiere a un grupo diverso de herramientas que utilizan tecnologías informáticas para mejorar la eficacia y la eficiencia de la industria de la salud.

La “eHealth” comprende varias tecnologías, como el uso de dispositivos móviles aplicados a la salud (“mHealth”), incluyendo diarios electrónicos, sensores ponibles o monitorización de la adherencia terapéutica; la informática biomédica (por ejemplo, la historia clínica electrónica, la prescripción electrónica o los sistemas de ayuda a las decisiones clínicas); la telemedicina, que es el uso de las tecnologías de la información y la comunicación para el manejo de enfermedades y de educación sanitaria; las plataformas de redes sociales, y el análisis de la información adquirida a través de estas plataformas, usando técnicas de “big data” o inteligencia de datos.

En esta revisión, resumimos la evidencia que rodea al uso de tecnologías “eHealth” y su relevancia para las enfermedades alérgicas.

Palabras clave: macrodatos; salud electrónica; salud móvil; redes sociales; telemedicina.

Abbreviations/acronyms:

App: application.

EAACI: European Academy of Allergy and Clinical Immunology.

ED: emergency department.

eHealth: electronic health.

IT: information technology.

mHealth: mobile health.

USA: United States of America.

WHO: World Health Organization.

Introduction:

The meaning of “eHealth” (short for electronic health) has been a matter of debate during the last decade [1]. The most widely accepted explanation dates to 2001, when it was defined as “an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies. In a broader sense, the term characterizes not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve health care locally, regionally, and worldwide by using information and communication technology” [2].

Regardless of an exact definition, eHealth, also known as medical informatics or health information technologies, is a diverse group of tools that commonly utilize computerized technologies in order to improve efficacy and efficiency of the health care industry [3] (Figure 1).

Adoption of new technologies is high among the general population in developed countries. In 2013, it was reported that 56% of adults in the United States owned a smartphone [4], while in 2016, 75% of the European households had mobile internet access [5].

Allergic diseases are common chronic conditions which can have life-long impact. Allergies are estimated to affect up to 20% of the general population, and the prevalence is growing, with recent recognition of an “allergy epidemic” [6]. Asthma, atopic dermatitis and food allergies are entities that require successful implementation of self-management plans and patient empowerment to have the highest quality of life with the least interference in daily activities. Unfortunately, for many reasons, this is difficult to achieve for many patients [7].

The availability of new technology grants both clinicians and patients the opportunity to compile data and receive feedback regarding key symptoms, risk behaviour and/or management. The implementation of smartphones and “apps” (short for applications), along with other electronic tools that can be applied to healthcare and a proper analysis of the data can be useful for improving routine management of allergic patients [8].

In this review, we summarize the evidence surrounding various eHealth platforms and its relevance to the specialty of Allergy and Immunology.

mHealth

Rapid technological advancements over the past decade have been applied to healthcare, towards both individuals and at the population level. Mobile health (mHealth) refers to the use of mobile devices (smartphones, sensors, wearable technology, telemedicine) in medical care. mHealth encompasses an evolving field of applications that will be discussed in more detail below. mHealth technology can be integrated into the management of virtually any chronic health condition, including asthma, food allergies, and allergic rhinitis, and has tremendous potential for improving care for patients across the world. The utility of mHealth varies widely, from simple electronic symptom diaries or reminder systems, to complex sensors that offer real time biofeedback to patients and comprehensive clinical information to healthcare providers or third party observers. Artificial intelligence can help decipher millions of data points collected through mHealth applications and assist providers or patients with medical decision-making. Technology has reached a point where the main barrier lies in limitations of the human imagination.

Naturally, the technological advances and promises of future applications have outpaced our ability to fully understand the benefits and limitations, as well as the challenges that may prevent widespread implementation [9]. Evidence supporting meaningful clinical

benefit from mHealth applications is generally lacking but this has not prevented companies from developing or recommending use of their products. In general, studies evaluating the use of mHealth in the management of chronic conditions such as asthma and diabetes still offer low quality design and outcome measures [10].

Studies conducted in adult patients with asthma have revealed improvement in symptom scores, increased attendance at office visits, and reduced emergency room utilization for patients who have used a combination of at home spirometry and simple message servicing [11,12]. A randomized prospective trial of a mHealth application in children with asthma did not demonstrate any difference in emergency room visits or hospitalizations during a 6-month period, but there was a reduction in urgent care visits [13].

At the time of this writing, there are over 300,000 mHealth applications available for anyone to download and use. In 2013, the United States Food and Drug Administration decided that mHealth applications will not be regulated unless they are classified as a Class II or III medical device, which generally includes some form of sensor or adaptor measuring clinical information. With no oversight, the breadth of mHealth offerings can be overwhelming and unreliable. Many applications may not be developed by healthcare experts or offer evidence-based information [14]. It is important for the entire healthcare industry, including practitioners, insurance providers, and especially patients to understand these limitations and thoughtfully consider mHealth in augmenting care. More than ever, the marketing of such technology must be balanced with clinical utility. Equally important, patient privacy must be fully protected, particularly if mHealth applications are designed to transmit private medical information to providers.

Wearables

According to recent advances in nanotechnology and wireless communication, one of the new facilities technology offers is also one of the most commonly employed: the use of wearable biosensors aimed to provide vital signs and monitoring of not only patients but also athletes and the general population [15] (Figure 2).

Although wearables have been applied for several health disorders [16], little is described related to allergic diseases. Regarding asthma, a device for identifying wheeze integrates measurements from different stethoscopes into diagnostic algorithms which aids at-home diagnosis of asthma [17]. A low power device, consisting of a wristband, a chest patch and a hand-held spirometer has been described to be able to monitor multiple variables, including ozone levels, temperature, humidity, wheezing and lung function. Its purpose is to improve management of chronic respiratory diseases, such as asthma. However, clinical utility has not been demonstrated as of yet [18]. A commercially available wrist-worn device developed to monitor sleep quality of children with asthma was studied and demonstrated favorable results, including adequate correlation with polysomnographic data [19].

Food allergy and anaphylaxis are conditions that could theoretically benefit from wearables technology. There are at least two projects surrounding anaphylaxis detector devices, which would act by measuring mast cell mediators, but their actual utility remains to be established [20]. There are several devices claiming to detect traces of offending foods in prepared meals, mostly targeting gluten for coeliac patients. In the case of food allergens, there is a patent for a food allergen detection method using molecularly imprinted polymers [21], which is being used for the development of a device that would detect peanuts, tree nuts, fish, shellfish, wheat, eggs, milk, and soy [22]. Unfortunately, at the time of this writing, there is no published evidence supporting such claims. Lastly, a “smart” case for epinephrine auto-injectors, linked to the user’s

smartphone, has demonstrated ability to improve management of anaphylaxis and decrease patients' anxiety [23].

Overall, studies are scarce and lack strength of methodological design and use of relevant outcome measures. Errors in detection of data are common, due to unconscious bias when developers apply a usual behaviour to a heterogeneous population. As such, researchers have the responsibility of determining inconsistencies in health apps and wearables [24].

Adherence systems

Thus far, we have reviewed several important aspects to consider regarding the utility and benefits of different mHealth platforms. Nonadherence is one area where mHealth may have the most potential to positively impact patient care [25]. It is well established that nonadherence is common among patients managing chronic medical conditions and takes many forms [26]. Patients with poorly controlled asthma often do not use their controller medications consistently or with proper inhaler technique [27]. Patients with food allergies frequently do not have their epinephrine autoinjector available at all times and even if available, fail to use it for treatment of anaphylaxis [28]. Nasal steroid sprays are the most effective therapy for treatment of chronic rhinitis but many patients fail to use them consistently, which minimizes benefit [29].

There are several potential ways that mHealth platforms can improve adherence (Table I). An important psychological aspect to consider is that individual response to various reminder systems can vary. Some people respond very well to a daily reminder or calendar approach to increase medication use on a consistent basis. However, reminder systems and alarms can have unintended consequences, particularly for patients who are not coping well with their chronic medical condition and do not want a constant reminder of their reliance on medications [11].

The long-term engagement and use of mHealth applications by patients is widely unknown. It is anticipated that most people will either lose interest or stop using their applications over time, unless they recognize the benefit and experience some positive reinforcement. Gamification uses elements found in game playing (point scoring, competition with others, unlocking rewards) as a way to increase user engagement. Variable reinforcement akin to playing slot machines can tie in with gamification to provide intermittent rewards to users. Ultimately, tangible rewards, e.g. gift cards or reduced cost of medications, may offer the best approach to maintain user engagement but this requires financial support. If more studies can demonstrate clinical efficacy of mHealth platforms, then insurance providers or third party payers may be more willing to finance rewards if clinically meaningful improvement and cost savings can be demonstrated, e.g. reduced asthma-related ED visits.

An evolution of simple reminder systems or alarms includes the use of sensors on medication bottles or inhalers [30]. Sensors can be programmed to turn certain colors or emit a reminder sound when the bottle has not been opened or inhaler expressed at a prespecified time. The benefit of these sensors is that they can most closely approximate actual use of the medication, whereas reminder alarms/medication logs only record patient reported use, but not actual use of the medication. An interesting aspect of sensors used in studies evaluating adherence with asthma inhalers demonstrates that patients enrolled in a clinical trial (and who know they are being monitored) self-report higher rates of adherence to medication compared with that detected by the sensor [31].

Ultimately, the most effective mHealth applications must include some aspects designed to help improve patient adherence. However, we need to gain a better understanding of how the various approaches may not only impact adherence but most importantly, how

they can be tailored towards individual patients. A one-size-fits-all approach will not likely be effective on a population basis.

Health informatics

Health informatics comprises a large number of other tools, including electronic health records, computerized physician order entry, clinical decision support systems and additional software solutions for administrative tasks.

Digitalization of health care in general, and Allergy/Immunology in particular, is expected to bring a number of benefits by improving quality, safety, efficiency and costs. However, adapting new information systems to health care has proven difficult and the scientific evidence supporting said effects is inconsistent [3,32].

The majority of the studies addressing these effects have focused on clinical decision support systems, reporting beneficial effects [33]. For example, a study of electronic health records-embedded alerts, performed in primary care paediatric centres, resulted in a substantial improvement of asthma management [34]. However, other studies have reported these systems to result in “alert fatigue” and unnecessary workflows [33].

Regarding the economical and efficiency-related benefits of health informatics, there is little to no evidence in the field of Allergy. In general health care, results are controversial, with cost effects ranging from a 75% decrease to a 69% increase, when accounting for cost of implementation [32]. More quality studies are expected to come regarding the economical evaluation of these systems.

Telemedicine

Telemedicine has several definitions but the World Health Organization (WHO) defines it as “the delivery of health care services, where distance is a critical factor, using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease, research and evaluation, and for the continuing education of health care providers” [35]. There are two modalities of telemedicine: store-and-forward and real-time interactive services. In the first modality, packets of data (radiographic images, peak expiratory flow rate recordings) are transmitted to a specialist who offers diagnostic or management advice. However, real-time interactive services involves real-time contact using IT technologies (telephone, video calling) [36]. Telemedicine is not only used to exchange medical information between professionals but is also used to remotely monitor patients with chronic conditions such as asthma, diabetes or skin conditions, improving overall health outcomes [36,37].

Telemedicine has several potential benefits, including cost reduction [37] by reducing the number of cancelled appointments and travel to the hospital. A 2014 study found that e-visits could save as much as \$5 billion, considering that an e-visit costs approximately \$40 compared with an in-person visit which costs \$73 [37,38].

In regard to allergic conditions, telemedicine has been used mostly in patients with asthma. The first report was published by Romano et al. and found a reduction in symptoms and improvement of the quality of life of 17 paediatric patients with asthma [39]. Afterwards, several studies have demonstrated how monitoring peak flow using short message system (SMS) [40] or internet-based systems [41], and providing education to patients using face-to-face real-time telemedicine [42], improves asthma outcomes, demonstrating to be comparable to in-person visits [43].

Another area of potential utility that has been investigated involves the use of telemedicine in triaging patients who require referral to the allergist for further evaluation. Krishna et al proposed four triaging models for allergic rhinitis, food allergy, chronic urticaria and suspected anaphylaxis discharged from the emergency department [36]. Finally, a recent study showed that telemedicine may be used to de-label penicillin-allergic patients, saving time and money (more than \$30000), and providing high satisfaction rates in patients [44].

Still, telemedicine has yet to be strongly validated. Limitations, such as lack of physical evaluation, are obvious and of the utmost importance in respiratory diseases. Satisfaction with telemedicine consultation due to respiratory tract infections has been reported to be high. However, it has also been reported that antibiotics are often overprescribed to these patients, despite the fact that antibiotics are rarely warranted in the treatment of these episodes. Moreover, patients who were prescribed antibiotics showed higher satisfaction rates [45,46].

Social media

The use of the internet, and social media in particular, as a source of health information, has increased in recent years. This has been described in several studies. A telephone survey conducted in the US in 2010, found that 15% of American adults use social media in order to gather health information [47]. A survey conducted by the European Commission in 2014, described that 59% of the respondents had used the internet to search for health-related information, while 17% searched information regarding a specific disease on social media [48]. In 2015, a survey led by the Spanish Government, demonstrated that 60.5% of adults use the internet for health-related purposes and 37.6% use social media in a similar fashion [49]. A recent study, based on a survey among food-

allergic patients attending a Spanish paediatric allergy unit, described that over two thirds of them used social media, most of them daily, and 25% used them to gather information related to their disease [50].

However, there are few studies evaluating the actual effect of social media and other similar online platforms in improving care for allergic conditions. Evidence supports a possible beneficial effect from use of these resources for patients with asthma [51,52]. A randomized clinical trial demonstrated that online reminders could increase asthma control among adults [53]. Yet, a paradoxical effect also seems possible [54–56], given the ease in which incorrect and potentially harmful information may be accessed [57,58].

One of the hampering factors for the use of social media in allergy and other healthcare disciplines is reliability. Only 14.7% of Spaniards consider social media as a trustworthy source for health-related information [49]. There is no standardized method to measure the quality of information available in social networks [59]. In the particular case of allergy and immunology, reliability of videos posted on YouTube™ has been found to be low for asthma, rhinitis, and immunodeficiencies [60].

The growing trend in the use of social media also applies in physicians' private and professional aspects of life. A survey of Australian physicians found that 74% used social media networks to some extent [61]. From the point of view of allergists and clinical immunologists, social media seems to be a useful tool, not limited to sharing information, but also covering research [62], increasing the impact of scientific literature [63] and more [60]. In the last few years, the number of English-speaking allergists with Twitter™ accounts grew by 470% between 2011 and 2012 [64], and their activity has been documented to be steadily growing during congresses in the USA [65] and Spain [66].

Interestingly, 65.8% of Australian physicians indicated they were hesitant to immerse themselves more fully in social media and online communication due to worries about public access and legal concerns [61]. Therefore, there is a clear need for guidance on the proper use of social media, which needs to be considered for all doctors that choose to be active in this realm. EAACI has recently updated their Code of Ethics by including an annex on social media use by allergists [67]. Some tips for allergists considering having a presence on social media are provided in tables II and III. These tips may additionally help allergists ‘safely’ navigate on social media should they decide to be active.

Big Data

The term “Big Data” refers to the recording and analysis of data sets which are so large, multidimensional, diverse and complex that traditional software solutions are not adequate to process them [68]. The advent of Big Data is the result of the development of novel technologies which surpass the capacity of paper-based information management [69]. These technologies have enabled new ways to identify adverse events, cluster patients and measure quality of care [70].

The application of Big Data to Allergy and Immunology research is resulting in the rapid transformation into a data intensive discipline, as investigators are generating increasingly large, complex, multidimensional, and diverse data sets [71]. Sources of Big Data in health care include some of the technologies described previously in this article, such as mobile devices, websites, social media platforms, wearables, etc., but also includes genome registries, patient registries, private or government health claims, electronic health records or pharmacy claims [72].

Given the complexity and heterogeneity of asthma and allergic diseases, a systems biology approach is attractive, as it has the potential to model the myriad connections and

interdependencies between genetic predisposition, environmental perturbations, regulatory intermediaries, and molecular sequelae that ultimately lead to diverse disease phenotypes and treatment responses across individuals [73].

In systems biology, large data sets collected by multiple modalities in populations, ideally with multiple dimensions of data for each individual, are used to generate networks that link phenotypic information to interdependent genetic, regulatory, metabolite, and environmental profiles. The resulting networks are used to predict behaviour of the trait and generate novel, biologically relevant information [74].

This approach is already being used to reach a better understanding of respiratory allergic diseases. The most common approach is to record data provided by the patients, either actively or passively, via wearables. Asthma was one of the first conditions to be included in the ResearchKit platform (Apple; Cupertino, CA, USA), an open source framework for research, which can obtain informed consent, collect questionnaires, collect biometric data, provide reminders and notifications and store it securely. The specifically purposed Asthma Health Application allowed a group of researchers to conduct the Asthma Mobile Health Study, which resulted in the collection of data of over 7,000 U.S. participants, 6,000 of which agreed to share their data publicly for further research [75]. Initial analysis of this data set detected increased reporting of asthma symptoms in regions affected by heat, pollen and wildfires [76].

Allergy Diary is a mobile phone application which collects data of allergic nasal, ocular and asthma symptoms, as well as medication use on a daily basis. During a two-year-period, they included data from over 4,000 patients totalling over 30,000 days. Analysis of this data led to the description of a previously unrecognized pattern of uncontrolled multimorbidity [77,78].

On the other hand, Big Data does not need to be based on data provided by the patients. A model using Twitter, Google Search and environmental sensors demonstrated to be able to predict the number of asthma ED visits near-real-time with 70% precision [79]. Simple approaches, such as using Google Trends searches of specific allergy-related queries has proven useful to identify different prevalences of allergic rhinitis symptoms in the European Union countries [80].

However, there are limitations in the ability to release, locate, integrate and analyse data generated by others [81]. The use of the software associated with data is often restricted by the lack of tools, accessibility and training. Improved statistical and mathematic models that can be integrated into patients' electronic medical records and tests that can be performed as point-of-care decisions are needed [82]. As the allergy/immunology field continues to evolve and mature, it is likely that these technologies will soon provide evidence-based decision support tools [83].

Finally, the proliferation of big data has already raised privacy concerns [84]. In the big data era, the notion of information ownership has blurred, because all the data-producing actions (from social media to physician visits) involve more than one actor with inalienable rights to the data. For this reason, accepted norms around privacy will most probably change in the near future [85]. Still, the potential utility of big data and the uncertainty about the future must not be an excuse for not maintaining standards of ethical research [86].

Summary:

Keeping up with ever-changing technology is of the utmost importance for Allergy researchers and clinical practitioners. eHealth systems have been developing for over a decade. Nevertheless, it is in the last few years that it is becoming widespread. This is

happening due to the advances in miniaturization and the generalization of Internet access. Application of these tools will undoubtedly affect the Allergy field, for health care professionals and patients alike. Despite this generalization, there is a long way to go to have solid evidence on the beneficial effects of these technologies. The quality of the evidence available for allergic diseases is still patchy and inconsistent.

We must not forget that allergic diseases have heterogeneous manifestations. For this reason, it is likely that what works for one disease may not work for the rest. Thus, it is important to ascertain what kind of intervention may be beneficial for each condition. In the same fashion, mHealth technologies or social media may have positive effects for a certain group of patients, but not for others. It will be important to identify which patients should be offered what options, along with clear expectations regarding benefits and risks.

One of the most important concerns of eHealth is privacy. It must be protected for all actors of health care, but especially for patients. Novel dynamics in data exchange, either for research or for the clinical practice, must always be accompanied by the highest standards of privacy protection methods.

Finally, it is important to note that most of the eHealth studies have been performed in first world countries, where access to novel technology is cheap and common. However, it is possible that developing countries might benefit even more from use of these technologies, due to the significant lack of facilities and trained health care professionals.

Tables:

Feature	Potential Benefit
Reminder systems	Assist patients who forget to take medication consistently
Point scoring/rewards	Make use of the application more fun and provide positive reinforcement to the user
Competition	Link medication use/symptoms with a social media platform that allows comparison with other users
Sleek appearance	Well-designed apps make it easier for users to navigate through all features
Feedback	Weekly updates within the app or through electronic messaging can promote ongoing engagement
Sensors	Unique design element that can provide reminders or reinforce medication use
Symptom diaries	Encourages ongoing engagement and potential for patients to review their progress
GPS activity trackers with environmental alerts	Offers real time assessment/feedback for patients regarding air quality or other environmental factors in regards to their exact location

Table I. mHealth elements designed to improve adherence.

- Social media is a method of building relationships with different parties (other doctors, members of the public, journalists, politicians and stakeholders [87].
- Actions online and content posted may negatively affect reputations among patients and colleagues and can undermine public trust in the medical profession [88].
- Once content is online, it is extremely difficult to remove it (if at all) and can thus quickly spread beyond one's control [89].
- Privacy settings do not guarantee that posts are not seen by a wider audience [67].
- The link between social media may blur the boundary between personal and professional identities [67].
- Interaction with patients within online public domains can be subjected to third-party scrutiny and misinterpretation [90].
- Anonymous patient specific information can still be linked to the particular patient. Optimal posts should include very general information [88].
- Defamers can be blocked and reported to the corresponding platform where the issue was raised.

Table II: Tips aimed at understanding the framework underlying social media.

- Distinguish private from professional presence and interaction online: Create individual private and professional accounts. Ignore patients’ “friendship requests” on private accounts; redirect them to professional accounts.
- Safeguard personal information and content: adjust privacy settings especially in relation to private social media accounts.
- Be conscious and cautious of the online image. Self-identify, including institution. Profile page should comply with the desired professional image.
- Maintain patients’ confidentiality: do not disclose patients’ information, avoid discussing complaints, do not acknowledge a physician-patient relationship online.
- Avoid providing specific medical advice online and encourage patients to address their health issues/concerns in person with an allergist.
- Adhere to updated institutional social media guidance that may apply in each individual case.

Table III: Rules aimed at maintaining digital professionalism. Adapted from EAACI Code of Ethics [67].

Figures:

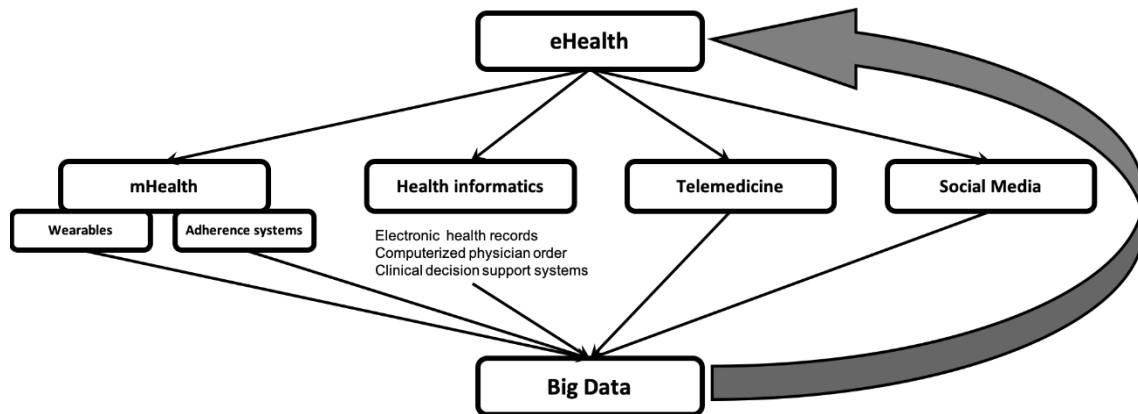


Figure 1: The term eHealth comprises different computerized tools. All of them can be used as a source of records for Big Data, which analysis would result in a better efficacy and efficiency of the system.

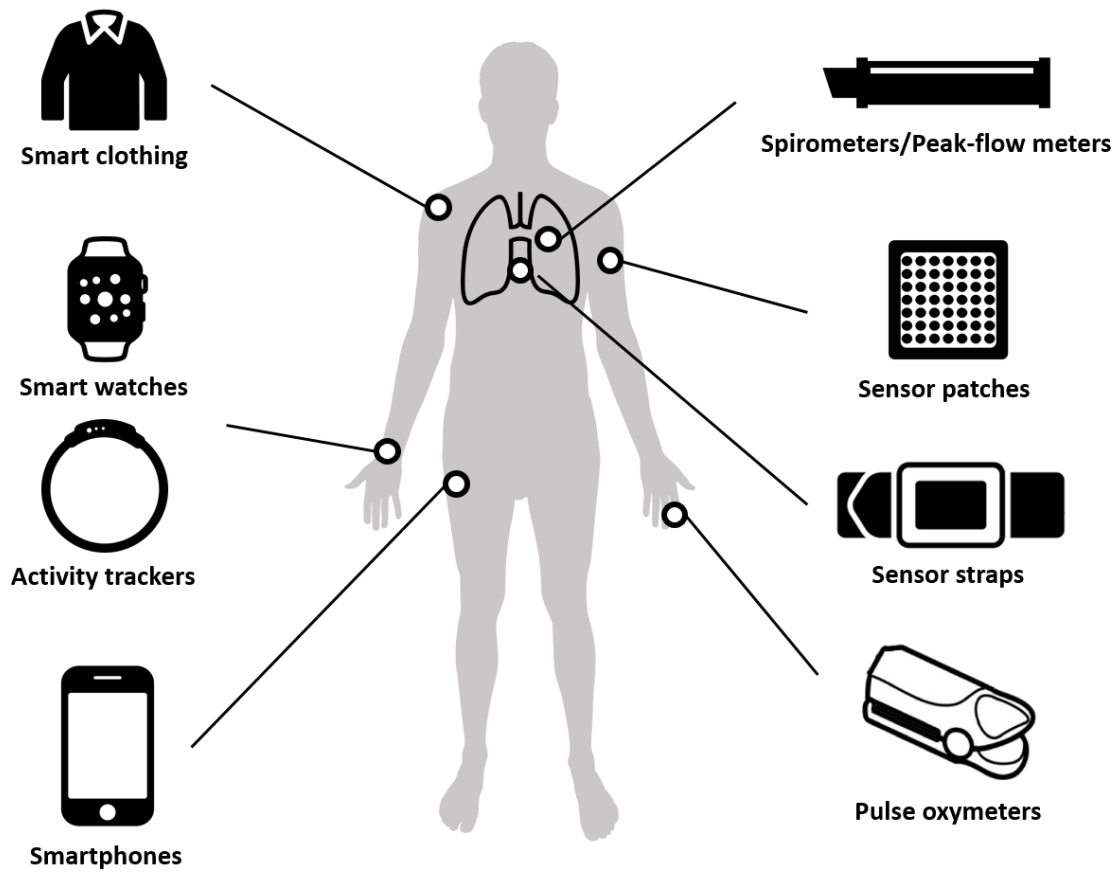


Figure 2: Available and potential sensors for use in wearables.

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